

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-163 are in this case. Claims 86-149 are withdrawn from consideration as being drawn to a non-elected invention. Claims 5-12, 14-15, 30-34, 36-41, 43-44, 61-64, 66-71, 73-74, 152 and 154-157 have been previously canceled. Claims 1-4, 13, 16-29, 35, 42, 45-60, 65, 72, 75-85, 150-151, 153 and 158-163 have been examined on the merits. Claims 1-4, 13, 16-29, 35, 42, 45-60, 65, 72, 75-85, 150-151, 153 and 158-163 have been rejected. Claims 16, 45, 55, 75, 84, 86-151 and 153 have now been canceled. Claims 1, 17-18, 26, 47, 49-50, 56-57, 77, 85 and 158-163 have now been amended.

The Examiner has acknowledged Applicant's amendment filed on August 22, 2005, wherein claims 1, 13, 16, 20-24, 25, 26, 42, 45, 46, 51-55, 57, 72, 75, 76, 79, 80-84, 150, 153, 158, 159, 160, 162 and 163 have been amended, and claims 5-12, 14, 15, 30-34, 36-41, 43, 44, 61-64, 66-71, 73-74, 152 and 154-157 have been canceled and has stated that this amendment was sufficient to overcome all the objections and rejections raised in the Official Action dated May 2, 2005.

The Examiner has further stated that Applicant's amendment necessitated the following new grounds of rejection: Claims 57-60, 72, 75-85, 150-151, 153 and 158-163 are rejected under 35 USC § 112 second paragraph. Claims 1-4, 13, 16-29, 35, 42, 45-56, 158-163 are rejected under 35 USC §102 (b) as being anticipated by Pusineri et al. (U.S. Patent No. 6,559,199, hereinafter also referred to as Pusineri). Claims 57-60, 65, 72, 75-85, 150-151, and 153 are rejected under 35 USC §103 (a) as being unpatentable over Pusineri et al. (U.S. Patent No. 6,559,199) as applied to claims 1-4, 13, 16-29, 35, 42, 45-56, 158-163 above, in view of Bosch et al. (U.S. Patent No. 6,017,515, hereinafter also referred to as Bosch). Claims 57-60, 65, 72, and 75-85 are rejected under 35 USC §103 (a) as being unpatentable over Green et al. (U.S. Patent No. 6,592,890, hereinafter also referred to as Green), and further in view of Boddie et al. (J. Dairy Sci. 79, 1996, 1683-

1688, hereinafter also referred to as Boddie) and Bosch at al. (U.S. Patent No. 6,017,515, *supra*).

35 U.S.C. § 112 second paragraph rejection

The Examiner has rejected claims 57-60, 72, 75-85, 150-151, 153 and 158-163 under 35 USC § 112 second paragraph, for containing the abbreviation "HPV", since the abbreviation cannot be used properly to identify any particular material or product. Claims 75, 84, 150-151 and 153 have now been canceled. Claims 26, 57, 158, 160 and 163 have now been amended.

Specifically, the Examiner has stated that an abbreviation (or trademark or trade name) is used to identify a source of goods, and not the goods themselves, in the present case, to identify or describe a particular virus, accordingly, the identification or description is indefinite and the claim scope is uncertain.

Claims 57, 158, 160 and 163 have now been amended to specifically recite "human papilloma virus" instead of the abbreviated term "HPV". In addition, claim 26 has been similarly amended, although not specifically rejected by the Examiner under this Item. Claims 75, 84, 150-151 and 153 have been canceled in view of the 102 and 103 rejections raised by the Examiner, as is detailed hereinunder.

Applicant believes that amended claims 26, 57, 158, 160 and 163 particularly point out and distinctly claim what Applicant regards as the invention and therefore, that amended claim 26, claims 27-29, 35, 42, 46-54 and 56 which depend therefrom, amended claim 57 and claims 58-60, 65, 72, 76-83 and 85, which depend therefrom, amended claim 158 and claim 159, which depend therefrom, amended claim 160 and claims 161-162, which depend therefrom, and amended claim 163, are no longer indefinite.

Applicant believes to have overcome the Examiner's rejection in this respect.

35 U.S.C. § 102 (b) rejection – Pusineri et al.

The Examiner has rejected claims 1-4, 13, 16-29, 35, 42, 45-56 and 158-163 under 35 USC §102(b) as being anticipated by Pusineri et al. (U.S. Patent No. 6,559,199).

The Examiner's rejections are respectfully traversed. Claims 16, 45 and 55 have now been canceled. Claims 1, 17-18, 26, 47, 49-50, 56 and 158-163 have now been amended.

Specifically, the Examiner has stated that Pusineri et al. disclose a composition comprising a silicone polymer and an antimicrobial agent such as chlorinated isocyanurate being entrapped in or by silicone polymer for destroying microbes. The Examiner has specified that Pusineri et al. disclose biocidal agents, such as N-chloro derivatives of cyanuric acids, trichloroisocyanuric acid, and sodium dichloroisocyanuric dihydrate. The Examiner has also specified that Pusineri et al. disclose silicone polymers which have properties such as fluidity, film forming ability, paste type rheologies etc. The Examiner has further specified that Pusineri et al. disclose a composition comprising a polyorganosiloxane composition which can be cross-linked or which is in the form of a cross-linked elastomer, and a biocidal agent, whereas the biocidal agents produce hypochlorous acid in the presence of water. The Examiner has further stated that the biocides used have destructive properties towards bacteria, viruses, fungi, yeast etc and that Pusineri et al. disclose that the active substance, such as a biocide, is incorporated inside the silicone matrix by homogenization. The Examiner has stated that the composition disclosed by Pusineri et al. can also comprise additives such as fillers, silicas, aluminas, sweeteners, saccharides etc. The Examiner has stated that the process for preparing the composition is also disclosed and that the compositions can be cross-linked at room temperature or by heat. The Examiner has stated that it is also disclosed that the compositions are compatible for contact with the skin and mucous membrane. In particular, the Examiner has stated that a composition comprising 20 parts by weight of bactericide is also disclosed therein.

The Examiner has concluded that the recitation of the intended use of the claimed invention, such as "for treating skin or mucosal membrane ailment caused by human papilloma virus", is not considered to limit the formulations claims herein, since "intended use" of a composition or product will not further limit claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same compounds (silicone polymer and chlorinated isocyanurate) in an effective amount, as the instantly claimed.

Pusineri et al. disclose a composition that is designed for taking dental impressions. As such, the composition is designed such that it is a fluid, non cross-linked composition, which hardens, via cross-linking in the oral cavity, thus forming the impression. More specifically, the composition includes a system of two polysiloxanes and a catalyst, which are mixed immediately prior to use, so as to be cross-linked in the oral cavity. This composition is thus composed of two non cross-linked polysiloxanes, whereby the cross-linking thereof is effected by the addition of a cross-linking agent to the composition and only once the composition is placed in the oral cavity (see, for example, a general description in columns 4-11, column 12, lines 9-44 and column 13, lines 34-41).

According to the teachings of Pusineri et al., the composition further includes a biocidal agent which is aimed at disinfecting the surface of the impression and/or of the intermass, and thus prevents surface or intermass contaminations by pathogenic microorganisms which lead to propagation and dissemination of microbes between the dental practice and the prosthetist's laboratory (see, for example, the section starting on column 1, line 66 and ending on column 2, line 4).

Further according to the teachings of Pusineri's et al., the distinct use of the composition taught therein imposes strict requirements of the various components of the composition: the polysiloxanes, the cross-linking agent and/or catalyst, the biocidal agent and additional components.

Thus, specific features of the polysiloxanes utilized within the composition are cited throughout the Pusineri et al. reference. First, a system of two polyorganosiloxanes (POS) is required. Second, the polyorganosiloxanes are selected such that they can be cross-linked therebetween, preferably via polyaddition (e.g., hydrosilylation) or polycondensation. Thus, the composition is selected so as to include, in one example, at least one diorganopolysiloxane having, per molecule, at least two alkenyl, preferably vinyl, groups linked to the silicone; at least one diorganopolysiloxane oil having, per molecule, at least three hydrogen atoms linked to the silicone; and a platinum catalyst. Additional examples and specific features of the polyorganosiloxanes of choice are widely described on columns 4-8 of the reference.

In addition to the careful selection of the polyorganosiloxanes used, Pusineri et al. further stress that the biocidal agent is selected such that it should not develop any inhibitory activity towards the crosslinking catalysts, and that the presence of the biocidal agent in the material should not interfere with or hamper the technical performance features of the elastomer material formed by the cross-linking; in particular, "the crosslinkability", the setting time, the rheological properties before crosslinking etc. (see, column 3, lines 35-45).

As described hereinabove, the biocide taught by Pusineri et al. is meant to act as a disinfecting agent, aimed at eliminating the presence of bacteria and other harmful organism on the dental impression, while transferring it from the dental clinic to the laboratory. The composition taught by Pusineri et al. is therefore not designed so as to slowly-release the biocide from the polysiloxane upon contacting the body, namely, the oral cavity.

Furthermore, the concentration of the biocidal agent is selected so as to suit its application in the oral cavity. While serving for preventive purposes, namely, to eliminate the presence of bacteria and other harmful organism on the dental impression, while transferring it from the dental clinic to the laboratory, the concentration of the biocidal agent utilized in the composition taught by Pusineri et al. is relatively low, being lower than 1 weight percent, preferably lower than 0.8 weight percent and more preferably lower than 0.5 weight percent (see, for example, column 4, lines 53-65).

In this respect, it should be stressed that contrary to the Examiner's remark, a composition comprising 20 parts by weight of bactericide is not disclosed by Pusineri et al., and although on column 14, line 51, there is disclosed a composition comprising a bactericide (II) solution containing 80 % by weight of calbenium (80 parts) in ethyl alcohol at 96 % (20 parts), the relative ratio of this component is thereafter defined to be as small as 1.25 %, 0.75 % or even 0.25 %.

The small amounts of biocidal agent used in practice by Pusineri et al. clearly stand in line with the preventive purposes of the biocidal agent and demonstrate that the biocidal agent is not aimed at exerting a therapeutic activity at infected areas.

The process of preparing the composition, as taught by Pusineri et al. describes mixing the two polyorganosiloxanes and the catalyst, which are altogether referred to as the POS composition (I), the biocidal agent (II) and any optional ingredients. In another particular, when describing the preparation of a composition suitable for taking dental impressions, the process comprises initiating crosslinking of the silicone elastomer, taking the dental impression and allowing the crosslinking to continue until the elastomer is hardened.

In sharp distinction, the present invention is of compositions comprising silicone polymers and an oxidizing agent (e.g., a chlorinated isocyanurate) being entrapped in or by the polymer. As is widely taught throughout the instant application, these compositions are designed so as to treat skin and mucosal ailments such as human papilloma virus (HPV), by releasing the oxidizing agent or an oxidizing moiety derived therefrom at the treated site (see, for example, the paragraph bridging pages 21 and 22 and the description starting at page 33 line 9 and ending at page 34 line 18). Thus, these compositions are designed so as to release the active oxidizing moiety upon hydration and/or diffusion, whereby the release profile can be controlled by pre-determining the properties of the carrier and the nature and amount of the oxidizing agent (see, for example, page 34, lines 14-18). Thus, for example, the polymer carrier can be designed such that chlorinated isocyanurate is slowly-released from the carrier by diffusion, and releases an active oxidizing moiety, namely, hypochlorous acid, by hydration upon contacting body fluids; or, alternatively, the polymer carrier can be designed such that the chlorinated isocyanurate is withheld within the polymer and releases an active oxidizing moiety, namely, hypochlorous acid, by hydration upon contacting body fluids within the polymer and the resulting hypochlorous acid then diffuses out of the polymer.

The sustained-release nature of the polymer is highly advantageous since it provides for continuous application of the therapeutic active agent (namely, the oxidizing agent or moiety) and avoids the need to use a repetitive treatment, as has been known so far in the treatment of skin and mucosal ailments.

As is further widely taught throughout the instant application, a preferred polymer that serves as a sustained-release carrier is a cross-linked silicone polymer (see, for

example, page 24, lines 13-15 and page 25, lines 1-4). Thus, contrary to the teachings of Pusineri et al., the polymer utilized in the composition according to the present invention is already a cross-linked silicone polymer and is not designed so as to be cross-linked upon its application, as is the composition taught by Pusineri et al. Moreover, by being designed so as to act as a sustained-release carrier of an oxidizing agent or moiety, the cross-linked polymer is selected capable of releasing the oxidizing agent or moiety upon hydration and/or diffusion, whereby a careful selection of the components composing the cross-linked polymer and their concentration, as taught by Pusineri et al., are not required.

Furthermore, by being designed to serve as a composition for treating skin ailments, the concentration of the active agent that is entrapped in or by the polymer is relatively large and suitable for therapeutic applications, and is particularly much higher than the concentrations used in the composition according to Pusineri et al., in which the biocide is used for preventive purposes. Thus, the oxidizing agent is present in the composition of the present invention at a concentration ranging between 10 weight percent and 90 weight percent, preferably between 20 weight percent and 80 weight percent, most preferably between 40 weight percent and 60 weight percent of the total weight of the composition (see, for example, page 31, lines 3-7). As is exemplified in the Examples section of the instant application, compositions containing 20 %, 40 %, 60 % and even 80 % of an oxidizing agent have been successfully prepared and practiced. Pusineri et al. clearly fails to teach compositions that contain such a high concentration of the biocidal agent taught therein.

The process of preparing the compositions taught in the present invention includes either cross-linking a mixture containing a silicone polymer and a chlorinated isocyanurate; and/or cross-linking a silicone polymer and then loading the polymerized silicone polymer with a chlorinated isocyanurate. While being prepared, the polymers can be designed as sheets, as tubulars, etc., whereby the oxidizing agent can be either entrapped within the polymeric matrix, spread over a surface of the matrix or entrapped between surfaces of polymer sheets, as is extensively discussed in the description of the present invention (see, for example, from page 31, line 10, to page 33, line 3). While the

composition as taught by Pusineri et al. is designed to be fluid prior to its application in the oral cavity, processes of preparing a composition as sheets or tubulars are not taught by Pusineri et al. and in fact are entirely not applicable for dental impressions.

In view of the above, it is clear that the composition described and claimed by the present invention is completely different from the composition taught by Pusineri et al. The differences between these compositions are inherent to the different uses of the two compositions and are as follows:

The composition taught by Pusineri et al., being designed for taking dental impressions, is meant to be used in its fluid, non cross-linked form, so as to be easily applied or brushed on the teeth, and includes a polycondensation catalyst, which is aimed at inducing cross-linking of the polymers in the composition, so as to enable the formation of the dental impression. The biocide contained within the composition is aimed merely at disinfecting the impression site, so as to allow the dental impression to arrive safely and hygienically from the dental practitioner to the prosthetist's laboratory, and thus the composition is not designed so as to slowly release this agent, to thereby exert a therapeutic activity at the treated area.

Contrary to the composition taught by Pusineri et al., the composition of the present invention comprises an already cross-linked polymer, which is designed so as to act as a sustained-release carrier, releasing an active agent upon hydration and/or diffusion. The silicone components of this composition are therefore not selected so as to be cross-linked upon application but are rather cross-linked in the first place, whereby the properties of the polymer are pre-determined according to the desired release profile of the active agent.

Notwithstanding the above, and in order to more clearly distinct the claimed invention from the teachings of Pusineri et al., Applicant has chosen to amend independent claim 1, to recite:

"[a] composition-of-matter comprising a pharmaceutical sustained-release carrier, said carrier comprising a biocompatible silicone polymer and a therapeutically effective amount of a chlorinated

isocyanurate for treating a skin or mucosal membrane ailment caused by a human papilloma virus, said chlorinated isocyanurate being entrapped in or by said polymer, and said polymer releasing said chlorinated isocyanurate upon hydration and/or diffusion.

Consequently, claim 16, which included the limitations now added to amended claim 1, has now been canceled. Claims 17 and 18, which previously depended from claim 16, have been amended to depend from claim 1.

In a similar manner, independent claim 26 has been amended to recite:

"[a] pharmaceutical composition comprising, as an active ingredient, a therapeutically effective amount of a chlorinated isocyanurate for treating a skin or mucosal membrane ailment caused by human papilloma virus, said chlorinated isocyanurate being entrapped in or by a pharmaceutical sustained-release carrier, said carrier comprises a cross-linked silicone polymer, wherein said polymer releases said chlorinated isocyanurate upon hydration and/or diffusion.

Consequently, claims 45 and 55, which included the limitations now added to amended claim 26, have now been canceled. Claims 47, 49 and 50, which previously depended from claim 45, have now been amended to depend from claim 26. Claim 56, which previously depended from claim 55, has now been amended to depend from claim 26.

Independent claim 158 has been similarly amended. Furthermore, in order to more clearly distinct the claimed invention from the teachings of Pusineri et al., Applicant has chosen to amend independent claim 158 and claim 159, which depend therefrom, independent claim 160 and claims 161-162, which depend therefrom, and independent claim 163, to replace the terms "polymerizing" and "polymerization" with the term "cross-linking". This amendment is fully supported in the specification, where it is clearly defined that the terms "condensation" and "cross-linking" refer to the

polymerization of silicone (see, for example, the section starting from page 42, line 17 until page 43, line 17, and the section starting from page 44, line 8 until page 45, line 2).

Thus, claim 158 has been amended to recite:

"[a] method of preparing a pharmaceutical composition for treating a skin or mucosal membranes ailment caused by human papilloma virus, the method comprising cross-linking a mixture of a silicone polymer and a chlorinated isocyanurate, so as to obtain said chlorinated isocyanurate entrapped within a cross-linked silicone polymer formed upon cross-linking, said cross-linked silicone polymer being a sustained-release carrier of said chlorinated isocyanurate and releases said chlorinated isocyanurate upon hydration and/or diffusion".

Claim 160 has been amended to recite:

"[a] method of preparing a pharmaceutical composition for treating a skin or mucosal membranes ailment caused by human papilloma virus, the method comprising cross-linking a silicone polymer so as to form a cross-linked polymerized silicone polymer and loading said polymerized silicone polymer with a chlorinated isocyanurate, so as to obtain said chlorinated isocyanurate entrapped within said polymerized silicone polymer, said cross-linked silicone polymer being a sustained-release carrier of said chlorinated isocyanurate and releases said chlorinated isocyanurate upon hydration and/or diffusion."

Claim 163 has been amended to recite:

"[a] method of preparing a pharmaceutical composition for treating skin or mucosal membranes ailments caused by human

papilloma virus, the method comprising cross-linking a silicone polymer and applying thereon a chlorinated isocyanurate, so as to obtain said chlorinated isocyanurate entrapped within said polymerized silicone polymer, said cross-linked silicone polymer being a sustained-release carrier of said chlorinated isocyanurate and releases said chlorinated isocyanurate upon hydration and/or diffusion"

As is argued hereinabove, Pusineri et al. fail to teach the compositions and processes of the claimed invention since Pusineri et al. fail to teach:

(i) a composition that comprises a cross-linked silicone polymer, entrapping an oxidizing agent and being a sustained-release carrier of the oxidizing agent, releasing the oxidizing agent upon hydration and/or diffusion; and

(ii) a process of preparing such a composition, in which cross-linking of a silicone polymer is effected ex-vivo, before applying the composition.

Applicant therefore strongly believes that amended independent claims 1, 26, 158, 160 and 163, as well as claims 2-4, 13, 17-25, 27-29, 35, 42, 46-54, 56, 159, 161 and 162, which directly or indirectly depend therefrom, are not anticipated by Pusineri et al. and are therefore allowable.

35 U.S.C. § 103 (a) rejection – Pusineri et al. in view of Bosch et al.

The Examiner has rejected claims 57-60, 65, 72, 75-85, 150-151 and 153 under 35 U.S.C. 103(a) as being unpatentable over Pusineri et al. (U.S. Patent No. 6,559,199) as applied to claims 1-4, 13, 16-29, 35, 42, 45-56, 158-163 above, in view of Bosch et al. (U.S. Patent No. 6,017,515). The Examiner's rejections are respectfully traversed. Claims 75, 84, 150, 151 and 153 have been canceled. Claims 57, 77 and 85 have been amended.

Specifically, the Examiner has stated that Pusineri et al. teach compositions comprising biocides, such as chlorinated isocyanurates, in a silicone polymer. Additionally, Pusineri et al. also teach that the biocidal silicone elastomer, in particular of room temperature vulcanization, is simple to obtain, is inexpensive, safe and compatible

for contact with skin, is effective from the point of antiseptic activity, and possesses excellent physical and chemical properties. Pusineri et al. also teach that such biocidal silicone compositions containing N-chlorinated compounds in the presence of water produce hypochlorous acid or salts of this acid, such as NaOCl, which have high bactericidal activity. It is further taught that the used biocides have destructive properties towards bacteria, viruses, fungi, yeast etc. The Examiner has stated that Pusineri et al. do not specifically teach a method of treating skin ailment caused by human papilloma virus using a composition comprising chlorinated isocyanurate.

Furthermore, the Examiner has stated that Bosch et al. (U.S. Patent No. 6,017,515) teach a method of treating skin disorders and mucous membrane ailments caused by human papilloma viruses, such as for example warts, comprising applying to the skin a composition comprising sodium hypochlorite, which is known to have bactericidal activity.

Thus, the Examiner has concluded that it would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the biocidal composition comprising chlorinated isocyanurate, in a silicone polymer taught by Pusineri et al. for the treatment of skin ailments caused by viruses, such as warts. The Examiner has further concluded that one of ordinary skill in the art, at the time of invention, would have been motivated to use the composition taught by Pusineri et al. for the treatment of warts because Pusineri et al. teach that the oxidizing agents, chlorine releasing compounds such as chlorinated isocyanurates are useful for treating diseases caused by viruses, fungi, bacteria etc., generally, and Bosch et al. teach that the chlorine releasing oxidizing agent, sodium hypochlorite, is used in the treatment of warts caused by human papilloma virus and that hence, one of ordinary skill in the art would have been motivated to use the biocidal silicone composition taught by Pusineri et al. for skin ailment such as warts because the biocidal silicone composition taught by Pusineri et al. on contact with water produces hypochlorous acid or salts of this acid, such as NaOCl, which are used in the treatment of warts.

As argued hereinabove, Pusineri et al. fail to teach a composition that comprises a cross-linked silicone polymer, entrapping an oxidizing agent and being a sustained-

release carrier of the oxidizing agent, releasing the oxidizing agent upon hydration and/or diffusion.

Bosch et al. teach two-component gel or paste systems for the bleaching of teeth and for the treatment of skin disorders and mucous membrane ailments, such as aphtae, lesions or warts. According to the teachings of Bosch et al., the treatment is effected by repetitive application of the composition. Thus, for example, in the treatment of aphtae, the composition of Bosch et al. is applied 6 times a day (see, column 6, lines 30-32), in the treatment of acne, it is applied 5 times a day (see, column 6, lines 34-37) and in the treatment of warts, it is applied 4 times a day (see, Example III). A plausible explanation of the need for repetitive application may lie in the limited amount of active ingredient which can be safely placed on the skin without damaging it, thus necessitating the repeated application of relatively small amounts of the oxidizing agent.

As extensively discussed throughout the instant application (see, for example, page 9 lines 2-6 and the paragraph bridging pages 21 and 22), the need for a prolonged application of the therapeutic agent in the treatment of skin ailments such as HPV is widely recognized, whereby as a result, commonly used compositions are indeed utilized while being repeatedly applied on the treated area. The present invention, however, is meant to overcome these recognized disadvantages of the known treatment methods by providing a composition that enables a continuous treatment without the need for repetitive application of the active ingredient.

Thus, in sharp contrast to the teachings of Bosch et al., the composition taught by present invention is designed so as to slowly release the active ingredient from a polymer carrier that is selected capable of serving as a sustained release carrier and further enables continuous application thereof on the treated area. The composition, as well as the method of treating HPV which utilizes this composition, are highly advantageous in that large amounts of an active ingredient can be loaded onto the polymer carrier, whereby an active moiety is slowly released from the carrier upon hydration and/or diffusion. Thus, the need for repeated applications is circumvented.

The whole concept of treating skin ailments such as warts caused by HPV by slow-releasing an oxidizing agent entrapped within a polymer carrier, is neither taught

nor suggested in Bosch et al. or Pusineri et al., since (i) Bosch et al. fail to teach the use of a polymer as a sustained release carrier of the active ingredient, and (ii) Pusineri et al. fail to teach a cross-linked silicone polymer that serves as a sustained release carrier of an active ingredient.

Notwithstanding the above, and in order to more clearly distinct the claimed invention from the teachings of Pusineri et al. and Bosch et al., Applicant has chosen to cancel claims 150, 151 and 153.

Applicant has further chosen to amend independent claim 57, to recite:

"[a] method of treating a skin or mucosal membranes ailment caused by human papilloma virus, the method comprising applying onto a treated region of the skin or mucosal membranes a therapeutically effective amount of a chlorinated isocyanurate being entrapped in or by a pharmaceutical sustained-release carrier, said carrier comprises a cross-linked biocompatible silicone polymer, wherein said biocompatible silicone polymer releases said chlorinated isocyanurate upon hydration and/or diffusion".

Consequently, claims 75 and 84, which included the limitations now added to amended claim 57, have now been canceled. Claim 77, which previously depended from claim 75, has now been amended to depend from claim 57. Claim 85, which previously depended from claim 84, has now been amended to depend from claim 57.

In view of the above, it is argued that a person skilled in the art would not have been motivated by the teachings of Bosch et al. and Pusineri et al. to incorporate an oxidizing agent in a silicone polymer which is designed so as to slowly release the oxidizing agent and to use such a composition in the treatment of warts.

Applicant therefore strongly believes that amended independent claim 57 as well as claims 58-60, 65, 72, 76-83 and 85, which directly or indirectly depend therefrom, are not rendered obvious by Pusineri et al. in view of Bosch et al. and are therefore allowable.

35 U.S.C. § 103 (a) rejection – Green et al. in view of Boddie et al. and Bosch et al.

The Examiner has rejected claims 57-60, 65, 72, and 75-85 under 35 U.S.C. 103(a) as being unpatentable over Green et al. (U.S. Patent No. 6,592,890), and further in view of Boddie et al. (J. Dairy Sci. 79, 1996, 1683-1688) and Bosch et al. (U.S. Patent No. 6,017,515). The Examiner's rejections are respectfully traversed. Claims 75 and 84 have now been canceled. Claims 57, 77 and 85 have now been amended.

Specifically, the Examiner has stated that Green et al. disclose a wound dressing composition having an anti-infective activity for treating skin ailments caused by microorganisms such as bacteria, comprising a sheet comprising a cross-linked polymer matrix, and oxidant generating formulation within or on the polymer matrix. The Examiner has stated that Green et al. also disclose that the oxidant generating formulation is stable at least until contacted by a substrate, such as glucose, which is permeable into the polymeric matrix from the patient's body fluid. The Examiner has stated that it is also disclosed that the wound dressing can be a single sheet having the oxidant generating formulation, or plurality of stacked sheets, having the same composition. The Examiner has stated that the conformable, flexible, and spreadable polymers such as cross-linked polymers of polyacrylamide, polyurea, polyurethane, polyvinylchloride, polyesters, polymethyl methacrylate, polytetrafluorethylene, elastomeric organosilicon polymers etc., and combination thereof are disclosed. The Examiner has stated that hydrophobic polymers (elastomers) include medical grade Low Consistency Silicone elastomers such as NuSil MED-815, High consistency Silicone Elastomers suitable for extrusion such as NuSil MED-4550, as well as thermoplastic and room temperature vulcanization (RTV) silicone polymers. The Examiner has stated that suitable anti-infective oxidizing agents disclosed are elemental iodine, hydrogen peroxide, hypohalites, hypothiocyanite etc. The Examiner has stated that it is also disclosed that oxidizing agents hypohalites, such as hypochlorites are formed upon wetting of the polymer in a body fluid. The Examiner has stated that a 4 % by weight of oxidizing agent iodate in the composition is also disclosed. The Examiner has stated that the data for anti-bacterial activity of oxidizing agent iodate in combination with iodide encapsulated silicone patches is also shown and that it is also disclosed that using a bilayer technique formulations of iodide and oxidizing agents of

iodide can be encapsulated in a thin polymer comprising the upper layer, and this allows the sustained release of iodide and the oxidizing agent over extended period of time. The Examiner has stated that thus, the oxidizing agent is entrapped in the silicone polymer. The Examiner has stated that it is further disclosed that the sponge like hydrogel composition containing oxidizing agent encapsulated in polymer can be fabricated into various shapes such as rolls, sheets etc. The Examiner has stated that disc shaped silicone devices containing the oxidizing agents in combination with NaCl were also prepared.

The Examiner has stated that Green et al. further teach a method of preparing a pharmaceutical composition, more specifically that finely ground oxidizing agent iodate and iodide were mixed into silicone elastomer and then the polymer was allowed to cure with dibutyl tin dilaurate catalyst. The Examiner has stated that bilayer technique is also disclosed, wherein the formulations of iodide and iodate, or other oxidizing agents of iodide, are encapsulated in a thin polymer of polyurethane or silicone comprising the upper layer, and combined with another film of polyurethane or silicone containing polymer. The Examiner has stated that Green et al. does not teach the particular oxidizing agent, chlorinated isocyanurate, entrapped in the silicone polymer, nor teach a method of treating skin ailment caused by human papilloma virus (HPV) using chlorinated isocyanurate entrapped in the silicone polymer.

The Examiner has stated that Boddie et al. disclose the use of oxidizing agent comprising a chlorinated isocyanurate in a similar formulation and a method of treating teat skin infected by microorganisms using said formulation. The Examiner has stated that Boddie et al. teach that teat dip formulations containing an oxidizing agent hypochlorous acid (a source of free chlorine), liberated from sodium dichloroisocyanurate in water by hydrolysis, were effective against bacteria such as *Staphylococcus aureus* and *Streptococcus agalactiae* IMI. The Examiner has stated that Boddie et al. further teach that sodium dichloroisocyanurate has a greater biocidal activity than sodium hypochlorite.

The Examiner has stated that Bosch et al. (U.S. Patent No. 6,017,515) teach a method of treating skin disorders and mucous membrane ailments caused by viruses, such

as for example warts comprising applying to the skin a composition comprising sodium hypochlorite.

Thus, the Examiner has concluded that it would have been obvious to a person of ordinary skill in the art, at the time of invention, to substitute oxidizing agent taught by Green et al. by another oxidizing agent, chlorinated isocyanurate, in the wound dressing composition of Green et al. for treating skin ailment because Boddie et al. teach teat dip formulation containing sodium isocyanurate for treating skin infections caused by bacteria. The Examiner has found that it would have been obvious to a person of ordinary skill in the art, at the time of invention, to use a composition comprising oxidizing agent, chlorinated isocyanurate, in a silicone polymer for the treatment of skin ailments caused by virus such as warts, because Bosch et al. teach that an oxidizing agent, sodium hypochlorite, is used in the treatment of warts. The Examiner has stated that one of ordinary skill in the art would have been motivated to use an oxidizing agent, such as chlorinated isocyanurate, with the expectation of obtaining a composition for the treatment of warts because chlorinated isocyanurate on contact with water produces hypochlorous acid, and hypochlorous acid is more potent germicide than sodium hypochlorite for treatment of microbial diseases. The Examiner has stated that one of ordinary skill in the art would have been motivated to use oxidizing agent comprising sodium isocyanurate entrapped in the polymer with the expectation of obtaining a pharmaceutical composition that allows the sustained release of oxidizing agent sodium isocyanurate over extended period of time as instantly claimed for the treatment of skin ailment caused by human papilloma virus.

As argued in detail hereinabove, the present invention teaches methods of treating skin ailments such as HPV, by utilizing a composition comprises a sustained-release polymeric carrier entrapping a chlorinated isocyanurate. As is discussed in detail hereinabove, these compositions are designed such that (i) the chlorinated isocyanurate is slowly-released from the carrier by diffusion, and releases an active oxidizing moiety, namely, hypochlorous acid, by hydration upon contacting body fluids; and/or (ii) the chlorinated isocyanurate releases an active oxidizing moiety, namely, hypochlorous acid,

by hydration upon contacting body fluids within the polymer and the resulting hypochlorous acid then diffuses out of the polymer.

Green et al. disclose compositions that require the inclusion of iodine as an essential active ingredient of the composition. Contrary to the present invention, Green et al. fail to teach (i) the use of a chlorinated isocyanurate as a therapeutically active agent; and (ii) that such a chlorinated agent, while being entrapped in a sustained-release silicone polymer, as is discussed in detail hereinabove, can be used in the treatment of skin ailments caused by HPV.

Boddie et al. teach a method of treating teat infection, which utilizes a chlorinated isocyanurate as an oxidizing agent that releases hypochlorous acid in water. While Boddie et al. teach a method of treating a teat infection, Boddie et al. fail to teach a method of treating a skin ailment. As is well-known in the art, teat infections typically involve internal infections, which can be reflected, *inter alia*, by skin symptoms. Furthermore, the specific teat infection cited by Boddie et al. is caused by certain bacteria. Boddie et al. are therefore completely silent with respect to treating infections caused by other microorganisms and further fail to teach skin ailments *per se*, that is, ailments that affect the skin itself.

Bosch et al. teach two component gel or paste systems for the bleaching of teeth and for the treatment of skin disorders and mucous membrane ailments, such as aphthae, lesions or warts. However, as argued hereinabove, Bosch et al. fail to teach compositions that are suitable for continuous application and further fail to teach a composition that comprises a sustained-release polymeric carrier entrapping a chlorinated isocyanurate.

Notwithstanding the above, and in order to more clearly distinct the claimed invention from the teachings of Green et al., Boddie et al. and Bosch et al., Applicant has chosen to amend independent claim 57, to recite:

"[a] method of treating a skin or mucosal membranes ailment caused by human papilloma virus, the method comprising applying onto a treated region of the skin or mucosal membranes a therapeutically effective amount of a chlorinated isocyanurate being entrapped in or by a

pharmaceutical sustained-release carrier, said carrier comprises a cross-linked biocompatible silicone polymer, wherein said biocompatible silicone polymer releases said chlorinated isocyanurate upon hydration and/or diffusion".

Consequently, claims 75 and 84, which included the limitations now added to amended claim 57, have now been canceled. Claim 77, which previously depended from claim 75, has now been amended to depend from claim 57. Claim 85, which previously depended from claim 84, has now been amended to depend from claim 57.

It is therefore argued that although Green et al. describe compositions that are designed to slowly release an oxidizing agent, and although Boddie et al. and Bosch et al. teach compositions for treating warts using a chlorinated isocyanurate as a therapeutically active oxidizing agent for treating warts, none of these references teaches the use of a composition that is designed to slowly release the oxidizing agent upon hydration and/or diffusion for treating warts caused by HPV and hence, that a person skilled in the art would not have been motivated by the teachings of Green et al., Bosch et al. and Boddie et al., alone or in combination, to incorporate a chlorinated isocyanurate in such a sustained release polymer carrier and to utilize this composition in the treatment of HPV, nor could a person skilled in the art have predicted that such a composition would be successfully prepared and practiced in the treatment of HPV.

Applicant is therefore of the opinion that any rejection in view of the combined teachings of Bosch et al., Green et al. and Boddie et al., is merely based on hindsight.

Applicant therefore strongly believes that amended independent claim 57, as well as claims 58-60, 65, 72 and 76-83 and 85, which directly or indirectly depend therefrom, are not rendered obvious by Green et al. in view of Boddie et al., and further in view of Bosch et al., and are therefore allowable.

In view of the above amendments and remarks it is respectfully submitted that amended claim 1, claims 2-4 and 13, amended claims 17-18, claims 19-25, amended claim 26, claims 27-29, 35, 42 and 46, amended claim 47, claim 48, amended claims 49-50, claims 51-54, amended claims 56-57, claims 58-60, 65, 72 and 76, amended claim 77, claims

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78-83, and amended claims 85 and 158-163, are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



Martin Moynihan
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Date: April 25, 2006

Enclosures:

A Petition for Two Month Extension of Time (1 Month Less Previously Paid);

A Request for Continued Examination (RCE)